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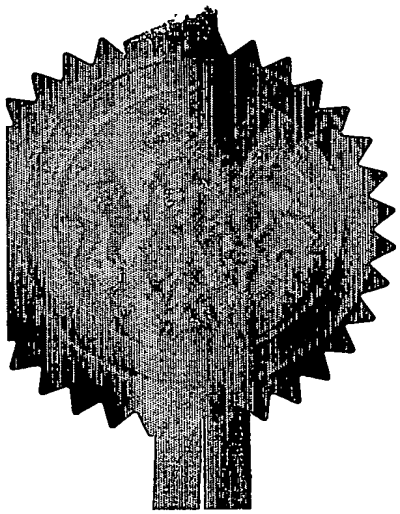

Signed Andrew Gorvett

Dated 22 April 2003

PCT/EP03/03195

Patents Form 1/77

Patents Act 1977
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The Patent Office

1/77

THE PATENT OFFICE
J
27 MAR 2002
LONDON

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
Cardiff Road
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1. Your reference — MG/HG/P33020

2. Patent application number
(The Patent Office will fill in his part) — 0207278.3

28MAR02 E707150-1 C69803
P01/7700 0.00-0207278.3

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Glaxo Group Limited
Glaxo Wellcome House, Berkeley Avenue,
Greenford, Middlesex UB6 0NN, Great Britain

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation — United Kingdom

4733587003

4. Title of the invention — Novel Compounds

5. Name of your agent *(if you have one)*

Corporate Intellectual Property

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

GlaxoSmithKline
Corporate Intellectual Property CN925.1
980 Great West Road
BRENTFORD
Middlesex TW8 9GS

Patents ADP number *(if you know it)*

8072555006

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer yes if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is named as an applicant, or
c) any named applicant is a corporate body
See note (d)

Patents Form 1/77

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Continuation sheets of this form	
Description	11
Claim(s)	2
Abstract	
Drawings	

10. If you are also filing any of the following, state how many against each item.

Priority Documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. We request the grant of a patent on the basis of this application

Signature _____ Date 27-Mar-02

S C Hockley

12. Name and daytime telephone number of person to contact in the United Kingdom

S C Hockley 01279 644355

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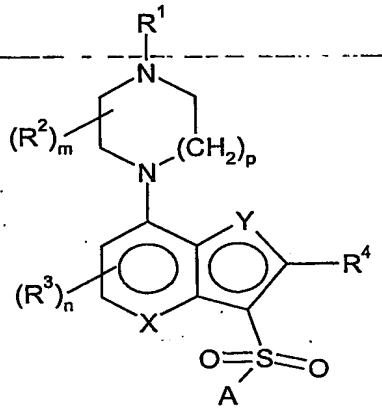
NOVEL COMPOUNDS

This invention relates to novel aza indole compounds having pharmacological activity, processes for their preparation, to compositions containing them and to their use in the treatment of CNS and other disorders.

WO 98/27081 discloses a series of aryl sulphonamide compounds that are said to be 5-HT_6 receptor antagonists and which are claimed to be useful in the treatment of various CNS disorders. GB-2341549, WO 99/47516 and WO 99/65906 all disclose a series of indole derivatives that are claimed to 5-HT_6 receptor affinity.

A structurally novel class of compounds has now been found which also possess affinity for the 5-HT_6 receptor. The present invention therefore provides, in a first aspect, a compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

one of X and Y represents –N= and the other represents –N(R^5)-;

R^1 and R^2 independently represent hydrogen or C_{1-6} alkyl or R^1 is linked to R^2 to form a group $(CH_2)_2$, $(CH_2)_3$ or $(CH_2)_4$;

R^3 independently represents hydrogen, halogen, cyano, -CF_3, -OCF_3, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkanoyl or a group –$CONR^6R^7$;

R^4 and R^5 independently represent hydrogen or C_{1-6} alkyl;

R^6 and R^7 independently represent hydrogen or C_{1-6} alkyl or together may be fused to form a 5- to 7- membered aromatic or non-aromatic heterocyclic ring optionally interrupted by an O or S atom;

m represents an integer from 1 to 4, when m is an integer greater than 1, two R^2 groups may instead be linked to form a group CH_2, $(CH_2)_2$ or $(CH_2)_3$;

n represents 1 or 2;

p represents 1 or 2

A represents a group –Ar^1 or – Ar^2Ar^3;

Ar^1, Ar^2 and Ar^3 independently represent an aryl group or a heteroaryl group, both of which may be optionally substituted by one or more (eg. 1, 2 or 3) substituents which may be the same or

different, and which are selected from the group consisting of halogen, hydroxy, cyano, nitro, trifluoromethyl, trifluoromethoxy, C_{1-6} alkyl, trifluoromethanesulfonyloxy, pentafluoroethyl, C_{1-6} alkoxy, arylC_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkoxyC_{1-6} alkyl, C_{3-7} cycloalkylC_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyloxy, C_{1-6} alkylsulfonylC_{1-6} alkyl, arylsulfonyl, arylsulfonyloxy, arylsulfonylC_{1-6} alkyl, C_{1-6} alkylsulfonamido, C_{1-6} alkylamido, C_{1-6} alkylsulfonamidoC_{1-6} alkyl, C_{1-6} alkylamidoC_{1-6} alkyl, arylsulfonamido, arylcarboxamido, arylsulfonamidoC_{1-6} alkyl, arylcarboxamidoC_{1-6} alkyl, aroyl, aroylC_{1-6} alkyl, arylC_{1-6} alkanoyl, or a group $CONR^8R^9$ or $SO_2NR^8R^9$, wherein R^8 and R^9 independently represent hydrogen or C_{1-6} alkyl or together may be fused to form a 5- to 7-membered aromatic or non-aromatic heterocyclic ring optionally interrupted by an O or S atom; or solvates thereof.

Alkyl groups, whether alone or as part of another group, may be straight chain or branched and the groups alkoxy and alkanoyl shall be interpreted similarly. Alkyl moieties are more preferably C_{1-4} alkyl, eg. methyl or ethyl. The term 'halogen' is used herein to describe, unless otherwise stated, a group selected from fluorine, chlorine, bromine or iodine.

The term "aryl" includes phenyl and naphthyl.

The term "heteroaryl" is intended to mean a 5-7 membered monocyclic aromatic or a fused 8-10 membered bicyclic aromatic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur. Suitable examples of such monocyclic aromatic rings include thienyl, furyl, pyrrolyl, triazolyl, imidazolyl, oxazolyl, thiazolyl, oxadiazolyl, isothiazolyl, isoxazolyl, thiadiazolyl, pyrazolyl, pyrimidyl, pyridazinyl, pyrazinyl and pyridyl. Suitable examples of fused aromatic rings include benzofused aromatic rings such as quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, cinnolinyl, naphthyridinyl, indolyl, indazolyl, pyrrolopyridinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzoxadiazolyl, benzothiadiazolyl and the like. Heteroaryl groups, as described above, may be linked to the remainder of the molecule via a carbon atom or, when present, a suitable nitrogen atom except where otherwise indicated above.

It will be appreciated that wherein the above mentioned aryl or heteroaryl groups have more than one substituent, said substituents may be linked to form a ring, for example a carboxyl and amine group may be linked to form an amide group.

Preferably, R^1 represents hydrogen or methyl, more preferably hydrogen.
Preferably R^2 represents hydrogen or methyl.
Preferably R^3 represents hydrogen, methyl or halogen.
Preferably R^4 and R^5 independently represent hydrogen or methyl.
Preferably m, n and p each represent 1.
When A represents a group $-Ar^1$, Ar^1 preferably represents optionally substituted phenyl or pyridyl, more preferably phenyl optionally substituted with halogen, cyano, trifluoromethyl or

trifluoromethoxy. Particularly preferred Ar^1 is phenyl optionally substituted with halogen (such as 2-fluorine).
When A represents a group $-Ar^2-Ar^3$, Ar^2 and Ar^3 preferably both independently represent phenyl or monocyclic heteroaryl group as defined above.
Preferably A represents a group $-Ar^1$.

Preferred compounds according to the invention include examples E1-E5 as shown below, or a pharmaceutically acceptable salt thereof.

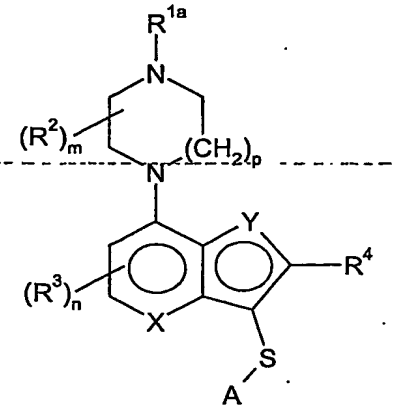
The compounds of formula (I) can form acid addition salts thereof. It will be appreciated that for use in medicine the salts of the compounds of formula (I) should be pharmaceutically acceptable. Suitable pharmaceutically acceptable salts will be apparent to those skilled in the art and include those described in J. Pharm. Sci., 1977, **66**, 1-19, such as acid addition salts formed with inorganic acids e.g. hydrochloric, hydrobromic, sulfuric, nitric or phosphoric acid; and organic acids e.g. succinic, maleic, acetic, fumaric, citric, tartaric, benzoic, p-toluenesulfonic, methanesulfonic or naphthalenesulfonic acid. The present invention includes within its scope all possible stoichiometric and non-stoichiometric forms.

The compounds of formula (I) may be prepared in crystalline or non-crystalline form, and, if crystalline, may optionally be solvated, eg. as the hydrate. This invention includes within its scope stoichiometric solvates (eg. hydrates) as well as compounds containing variable amounts of solvent (eg. water).

Certain compounds of formula (I) are capable of existing in stereoisomeric forms (e.g. diastereomers and enantiomers) and the invention extends to each of the stereoisomeric forms and to mixtures thereof including racemates. The different stereoisomeric forms may be separated one from the other by the usual methods, or any given isomer may be obtained by stereospecific or asymmetric synthesis. The invention also extends to any tautomeric forms and mixtures thereof.

The present invention also provides a process for the preparation of a compound of formula (I) or a pharmaceutically acceptable salt thereof, which process comprises:

(a) oxidation of a compound of formula (II)



(II)

wherein R^{1a} is as defined for R^1 or an *N*-protecting group and X, Y, R^2, R^3, R^4, m, n, p and A are as defined above and thereafter as necessary removing an R^{1a} *N*-protecting group; or

(b) deprotecting a compound of formula (I) which is protected; and thereafter optionally

(c) interconversion to other compounds of formula (I) and/or forming a pharmaceutically acceptable salt and/or solvate.

The *N*-protecting group used may be any conventional group e.g. *t*-butyloxycarbonyl (Boc) or benzyloxycarbonyl.

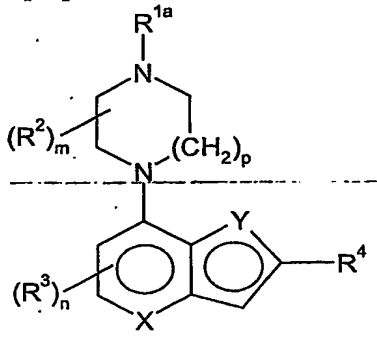
Process (a) typically comprises the use of an oxidising agent such as a peracid (e.g. 3-chloroperbenzoic acid or peracetic acid) or potassium monoperoxysulphate, in a suitable solvent such as dichloromethane or aqueous methanol.

In processes (a) and (b), examples of protecting groups and the means for their removal can be found in T. W. Greene 'Protective Groups in Organic Synthesis' (J. Wiley and Sons, 1991). Suitable amine protecting groups include sulphonyl (e.g. tosyl), acyl (e.g. acetyl, 2',2',2'-trichloroethoxycarbonyl, benzyloxycarbonyl or t-butoxycarbonyl) and arylalkyl (e.g. benzyl), which may be removed by hydrolysis (e.g. using an acid such as hydrochloric acid) or reductively (e.g. hydrogenolysis of a benzyl group or reductive removal of a 2',2',2'-trichloroethoxycarbonyl group using zinc in acetic acid) as appropriate. Other suitable amine protecting groups include trifluoroacetyl ($-COCF_3$) which may be removed by base catalysed hydrolysis or a solid phase resin bound benzyl group, such as a Merrifield resin bound 2,6-dimethoxybenzyl group (Ellman linker), which may be removed by acid catalysed hydrolysis, for example with trifluoroacetic acid. A further amine protecting group includes methyl which may be removed using standard methods for N-dealkylation (e.g. 1-chloroethyl chloroformate under basic conditions followed by treatment with methanol).

Process (c) may be performed using conventional interconversion procedures such as epimerisation, oxidation, reduction, alkylation, nucleophilic or electrophilic aromatic

substitution, ester hydrolysis or amide bond formation. For example, *N*-dealkylation of a compound of formula (I) wherein R^1 represents an alkyl group to give a compound of formula (I) wherein R^1 represents hydrogen. It will be appreciated that such interconversion may be interconversion of protected derivatives of formula (I) which may subsequently be deprotected following interconversion. It will also be appreciated that attempted conversion of optionally protected compounds of formula (I) wherein R^5 represents hydrogen into other optionally protected compounds of formula (I) wherein R^5 represents C_{1-6}alkyl using conventional alkylation methods may give rise to mixtures containing varying amounts of the corresponding regioisomers. Such mixtures may be separated by conventional means, for example using flash chromatography.

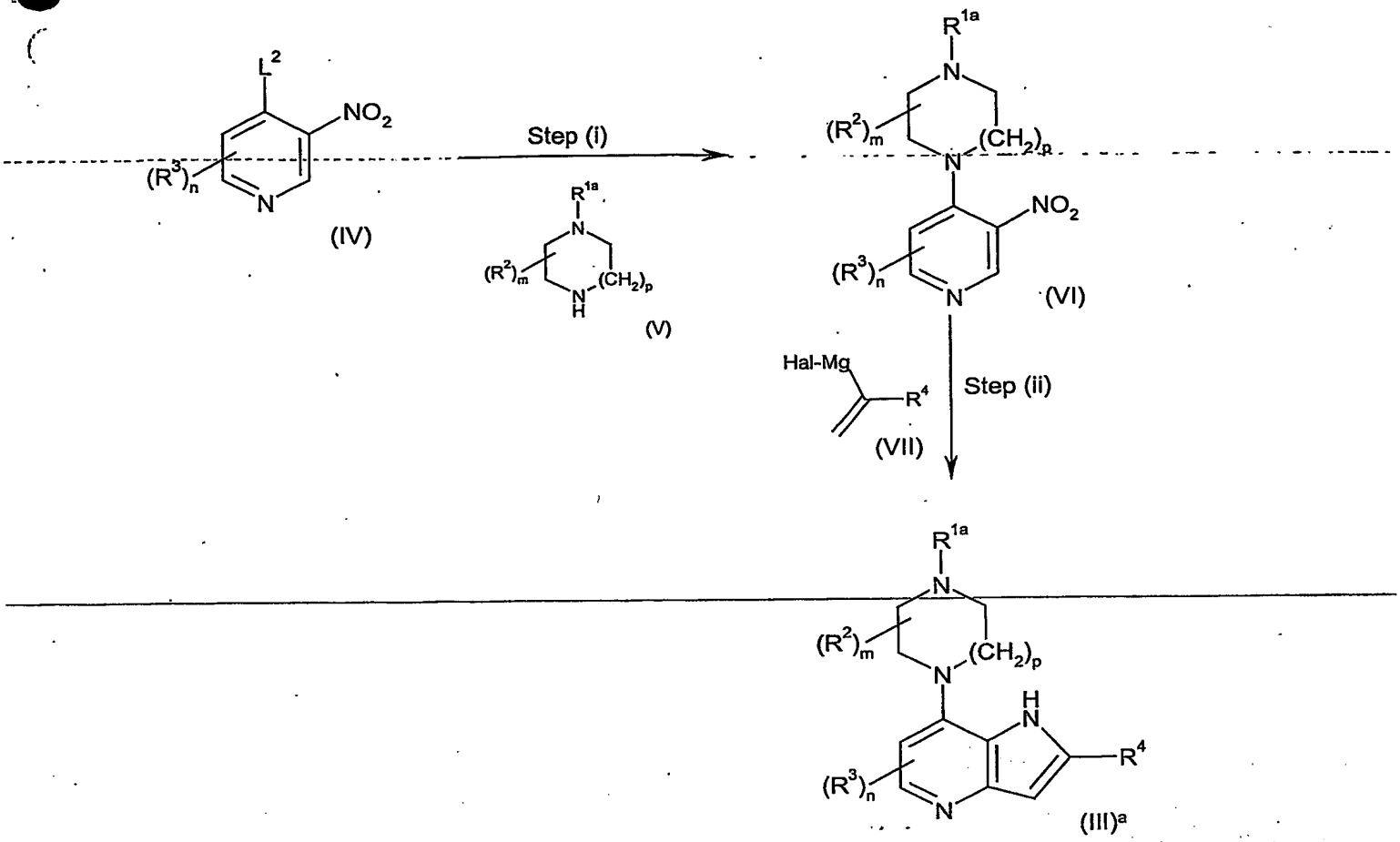
Compounds of formula (II) may be prepared by reacting a compound of formula (III)



(III)

wherein R^{1a} is as defined for R^1 or an *N*-protecting group and X, Y, R^2, R^3, R^4, m, n and p are as defined above, with a compound of formula A-S-L^1 or A-S-S-A, wherein A is as defined above and L is a leaving group such as halogen or methylsulfonyl. This reaction typically comprises the use of a base, for example in the case where X represents –N=, Y represents –N(R^5)- and R^5 represents hydrogen, a metal hydride (eg. sodium hydride) in a suitable solvent such as *N,N*-dimethylformamide which is then allowed to react with the compound of formula A-S-L^1 or A-S-S-A.

Compounds of formula (III) wherein X represents –N=, Y represents –N(R^5)- and R^5 represents hydrogen may be prepared in accordance with the following process:



wherein R^{1a} is as defined for R^1 or an *N*-protecting group and R^2, R^3, R^4, m, n and p are as defined above, L^2 represents a suitable leaving group such as halogen (eg. chlorine), Hal is a halogen atom such as chlorine or bromine.

Step (i) typically comprises the use of a base such as triethylamine or an excess of the compound of formula (V) and an inert solvent such as dichloromethane.

Step (ii) typically comprises the use of an inert solvent such as tetrahydrofuran at a suitable temperature (e.g. –40 °C).

Compounds of formula (IV), (V) and (VII) are known in the literature or can be prepared by analogous methods.

Pharmaceutically acceptable salts may be prepared conventionally by reaction with the appropriate acid or acid derivative.

Compounds of formula (I) and their pharmaceutically acceptable salts have affinity for the 5-HT_6 receptor and are believed to be of potential use in the treatment of certain CNS disorders such as anxiety, depression, epilepsy, obsessive compulsive disorders, migraine, cognitive memory disorders (e.g. Alzheimers disease, age related cognitive decline and mild cognitive impairment),

Parkinsons Disease, ADHD (Attention Deficit Disorder/Hyperactivity Syndrome), sleep disorders (including disturbances of Circadian rhythm), feeding disorders such as anorexia and bulimia, panic attacks, withdrawal from drug abuse such as cocaine, ethanol, nicotine and benzodiazepines, schizophrenia, and also disorders associated with spinal trauma and/or head injury such as hydrocephalus. Compounds of the invention are also expected to be of use in the treatment of certain GI (gastrointestinal) disorders such as IBS (Irritable Bowel Syndrome). Compounds of the invention are also expected to be of use in the treatment of obesity.

Thus the invention also provides a compound of formula (I) or a pharmaceutically acceptable salt thereof, for use as a therapeutic substance, in particular in the treatment or prophylaxis of the above disorders. In particular the invention provides for a compound of formula (I) or a pharmaceutically acceptable salt thereof, for use in the treatment of depression, anxiety, obesity and cognitive memory disorders

The invention further provides a method of treatment or prophylaxis of the above disorders, in mammals including humans, which comprises administering to the sufferer a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

In another aspect, the invention provides the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for use in the treatment or prophylaxis of the above disorders.

In order to use the compounds of formula (I) in therapy, they will normally be formulated into a pharmaceutical composition in accordance with standard pharmaceutical practice. The present invention also provides a pharmaceutical composition, which comprises a compound of formula (I) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

A pharmaceutical composition of the invention, which may be prepared by admixture, suitably at ambient temperature and atmospheric pressure, is usually adapted for oral, parenteral or rectal administration and, as such, may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, reconstitutable powders, injectable or infusable solutions or suspensions or suppositories. Orally administrable compositions are generally preferred.

Tablets and capsules for oral administration may be in unit dose form, and may contain conventional excipients, such as binding agents, fillers, tabletting lubricants, disintegrants and acceptable wetting agents. The tablets may be coated according to methods well known in normal pharmaceutical practice.

Oral liquid preparations may be in the form of, for example, aqueous or oily suspension, solutions, emulsions, syrups or elixirs, or may be in the form of a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, emulsifying agents, non-aqueous vehicles

(which may include edible oils), preservatives, and, if desired, conventional flavourings or colourants.

For parenteral administration, fluid unit dosage forms are prepared utilising a compound of the invention or pharmaceutically acceptable salt thereof and a sterile vehicle. The compound, depending on the vehicle and concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions, the compound can be dissolved for injection and filter sterilised before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilization cannot be accomplished by filtration. The compound can be sterilised by exposure to ethylene oxide before suspension in a sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

~~The composition may contain from 0.1% to 99% by weight, preferably from 10 to 60% by~~ weight, of the active material, depending on the method of administration.

The dose of the compound used in the treatment of the aforementioned disorders will vary in the usual way with the seriousness of the disorders, the weight of the sufferer, and other similar factors. However, as a general guide suitable unit doses may be 0.05 to 1000 mg, more suitably 0.05 to 200 mg, for example 20 to 40 mg, and such unit doses will preferably be administered once a day, although administration more than once a day may be required; and such therapy may extend for a number of weeks or months.

All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.

The following Descriptions and Examples illustrate the preparation of compounds of the invention.

Description 1

4-(4-*tert*-Butyloxycarbonyl)piperazin-1-yl-3-nitropyridine (D1)

To a stirred suspension of 4-chloro-3-nitropyridine [Carceller *et al.*, *J. Med. Chem.* 1996 *39* 487] (23.37 g, 0.147 mol) in dichloromethane (500 ml) under argon was added Et_3N (22.43 ml), followed by 1-Boc-piperazine (30.38 g, 0.14 mol). The reaction was left to stir for 72 h at room temperature. The solvent was then evaporated *in vacuo* and the residues partitioned between dichloromethane (250 ml) and water (250 ml). The organic layer was then washed with 10% citric acid (250 ml), sat. $NaHCO_3$ (250 ml), brine (250 ml), dried ($MgSO_4$) and the solvents evaporated *in vacuo* to give the product as a dark yellow solid (D1) (45 g)

NMR (DMSO-d_6) : δ_H 1.42 (9H, s), 3.24-3.26 (4H, m), 3.46-3.47 (4H, m), 7.17-7.18 (1H, d), 8.38-8.39 (1H, d), 8.79 (1H, s)

Description 2

7-(4-*tert*-Butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*]pyridine (D2)

To a solution of 4-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-3-nitropyridine (D1) (6.3 g, 20.5 mmol) in tetrahydrofuran (200 ml) at -50 °C under argon was added vinyl magnesium bromide (1M in THF; 67.4ml, 67.4 mmol) was added rapidly, keeping the temperature below - 40 °C. Reaction stirred at – 40 °C for 30 min, then poured into sat. NH_4Cl (1000 ml) and extracted with dichloromethane (2 x 500 ml). The combined organic layers were then dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification by flash chromatography (MeOH / dichloromethane) gave the product as a brown solid (D2) (2.3 g).

NMR ($CDCl_3$) : δ_H 1.49 (9H, s), 3.35-3.39 (4H, m), 3.64-3.68 (4H, m), 6.59-6.61 (1H, d), 6.66-6.67 (1H, d), 7.39-7.41 (1H, d), 8.25-8.27 (1H, d), 11.45 (1H, br s)

Mass Spectrum: $C_{16}H_{22}N_4O_2$ requires 302; found: 303 (MH^+)

Description 3

3-Phenylsulfanyl-7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*] pyridine (D3)

Sodium hydride (60% in mineral oil, 39.7 mg, 0.99 mmol) was washed in hexane and then taken up in dimethylformamide (4 ml). 7-(4-*tert*-Butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*]pyridine (D2) (200 mg, 0.66 mmol) was added and left to stir for 10min. Diphenyldisulfide (159 mg, 0.73 mmol) was added and the reaction left to stir for 16 h. The reaction mixture was then diluted with water (10 ml) and extracted with ethyl acetate (3 x 20 ml). The combined organic extracts were washed with water (50 ml), dried ($MgSO_4$) and the solvents evaporated *in vacuo*. Purification by flash chromatography (MeOH : DCM) gave the product as an off-white solid (D3) (115.3 mg).

NMR ($CDCl_3$) : δ_H 1.49 (9H, s), 3.35-3.39 (4H, m), 3.64-3.68 (4H, m), 6.58-6.61 (1H, d), 6.99-7.12 (5H, m), 7.63 (1H, s), 8.22-8.24 (1H, d), 12.45 (1H; br s).

Mass Spectrum: $C_{22}H_{26}N_4O_2S$ requires 410; found: 411 (MH^+)

Description 4

3-Phenylsulfonyl-7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*] pyridine (D4)

To a stirred solution of 3-phenylsulfanyl-7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*] pyridine (D3) (50 mg, 0.12 mmol) in methanol (5 ml) was added potassium monopersulfate (150 mg, 0.24 mmol) in water (1 ml). The reaction mixture was stirred for 90 min and the solvents evaporated *in vacuo*. The residue was partitioned between dichloromethane (10 ml) and sat. $NaHCO_3$ solution (10 ml). The aqueous layer was re-extracted with dichloromethane and the combined organic extracts dried ($MgSO_4$) and the solvents evaporated *in vacuo* to give the product as a white solid (D4) (54.2 mg).

NMR ($CDCl_3$) : δ_H 1.47 (9H, s), 3.67-3.70 (4H, m), 3.90-4.30 (4H, br m), 6.46-6.48 (1H, d), 7.44-7.52 (3H, m), 7.85 (1H, br s), 7.95-8.00 (3H, m), 10.50 (1H, br s)

Mass Spectrum: $C_{22}H_{26}N_4O_4S$ requires 442; found: 441 (M-H)

Descriptions 5 and 6

7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-4-methyl-3-phenylsulfonyl-4*H*-pyrrolo[3,2-*b*] pyridine (D5) and 7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1-methyl-3-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*] pyridine (D6)

To a stirred solution of 3-phenylsulfonyl-7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*] pyridine (D4) (52.7 mg, 0.12 mmol) in ethanol (4 ml) was added potassium hydroxide (8.5 mg, 0.18 mmol). After 20min, the solvent was evaporated *in vacuo* and the residue re-dissolved in acetone (2 ml). Dimethyl sulfate (15 mg, 0.12 mmol) was then added and reaction stirred for 2 h. The reaction mixture was diluted with dichloromethane (10 ml) and washed with water (10 ml), dried ($MgSO_4$) and the solvents evaporated *in vacuo*. Purification by flash chromatography (EtOAc : dichloromethane) gave 7-(4-*tert*-butyloxycarbonyl) piperazin-1-yl-4-methyl-3-phenylsulfonyl-4*H*-pyrrolo[3,2-*b*] pyridine (D5) (8.8 mg) and 7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1-methyl-3-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*] pyridine (D6) (26 mg) as brown oils.

7-(4-*tert*-butyloxycarbonyl) piperazin-1-yl-4-methyl-3-phenylsulfonyl-4*H*-pyrrolo [3,2-*b*] pyridine (D5):

NMR ($CDCl_3$) : δ_H 1.49 (9H, s), 3.00 (4H, br s), 3.82 (4H, br s), 4.11 (3H,s), 6.28-6.30 (1H, d), 7.29 (1H, s), 7.44-7.51 (3H, m), 7.87-7.89 (2H, m), 8.17 (1H, s)

Mass Spectrum: $C_{23}H_{28}N_4O_4S$ requires 456; found: 457 (MH^+)

7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1-methyl-3-phenylsulfonyl-1*H*-pyrrolo [3,2-*b*] pyridine (D6):

NMR ($CDCl_3$) : δ_H 1.49 (9H, s), 3.00 (4H, br s), 3.50 (4H, br s), 4.11 (3H,s), 6.82-6.83 (1H, d), 7.44-7.51 (3H, m), 7.84 (1H, s), 8.27-8.29 (2H, m), 8.49-8.51 (1H, d)

Mass Spectrum: $C_{23}H_{28}N_4O_4S$ requires 456; found 457 (MH^+)

Example 1

4-(3-Phenylsulfonyl-1*H*-pyrrolo[3,2-*b*]pyridin-7-yl)-piperazine hydrochloride (E1)

3-Phenylsulfonyl-7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1*H*-pyrrolo[3,2-*b*] pyridine (D4) (51 mg, 0.12 mmol) was taken up in 4*M* HCl (5 ml) and heated to 60 °C for 60min. The solvent was evaporated *in vacuo* to give the product as a white solid (E1) (39.8 mg)

NMR (CD_3OD) : δ_H 3.48-3.53 (4H, m), 4.05-4.08 (4H, m), 7.18-7.20 (1H, d), 7.58-7.69 (3H, m), 8.12-8.15 (2H, m), 8.28-8.30 (1H, d), 8.47 (1H, s).

Mass Spectrum: $C_{17}H_{18}N_4O_2S$ requires 342; found: 343 (MH^+)

Example 2

4-Methyl-7-piperazin-1-yl-3-phenylsulfonyl-4*H*-pyrrolo[3,2-*b*] pyridine (E2)

7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-4-methyl-3-phenylsulfonyl-1*H*-pyrrolo [3,2-*b*] pyridine (D5) was taken up in 4*M* HCl (1 ml) and heated to 60 °C for 1 h. Solvents were evaporated *in vacuo* to yield a brown solid (E2) (6.9 mg)

NMR (CD_3OD) : δ_H 3.53-3.55 (4H, m), 4.01-4.04 (4H, m), 4.28 (3H, s), 7.18-7.20 (1H, d), 7.60-7.75 (3H, m), 7.98-8.00 (2H, d), 8.27-8.29 (1H, d), 8.46 (1H, s)

Mass Spectrum: $C_{18}H_{20}N_4O_2S$ requires 356; found 357 (MH^+)

Example 3

1-Methyl-7-piperazin-1-yl-3-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*] pyridine (E3)

7-(4-*tert*-butyloxycarbonyl)piperazin-1-yl-1-methyl-3-phenylsulfonyl-1*H*-pyrrolo [3,2-*b*] pyridine (D6) (58.9 mg) was taken up in 4*M* HCl (6 ml) and heated to 60 °C for 60 min. Solvents evaporated *in vacuo* to yield an orange solid (E3) (50.2 mg)

NMR (CD_3OD) : δ_H 3.54 (4H, br s), 3.76 (4H, br s), 4.20 (3H, s), 7.44-7.46 (1H, d), 7.56-7.69 (3H, m), 8.11-8.14 (2H, d), 8.47-8.49 (1H, d), 8.60 (1H, s)

Mass Spectrum: $C_{18}H_{20}N_4O_2S$ requires 356; found 357 (MH^+)

The following Examples (E4-E5) were prepared using an analogous method to that used for Examples E1–E3.

Example 4

1-Methyl-7-piperazin-1-yl-3-(2-fluorophenyl)sulfonyl-1*H*-pyrrolo[3,2-*b*] pyridine (E4)

~~Mass Spectrum: $C_{18}H_{19}FN_4O_2S$ requires 374; found 375 (MH^+)~~

Example 5

4-Methyl-7-piperazin-1-yl-3-(2-fluorophenyl)sulfonyl-4*H*-pyrrolo[3,2-*b*] pyridine (E5)

Mass Spectrum: $C_{18}H_{19}FN_4O_2S$ requires 374; found 375 (MH^+)

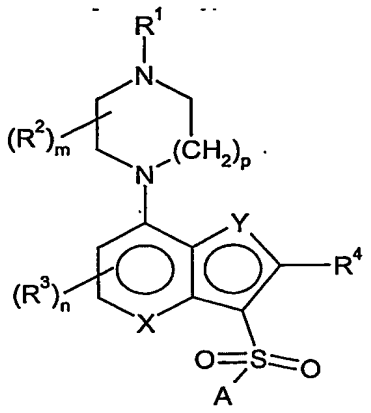
Pharmacological data

Compounds can be tested following the procedures outlined in WO98[illegible]

The compounds of Examples E1-E5 were tested and showed good affin[illegible] the 5-HT[illegible]ptor; having pKi values > 7.0 at human cloned 5-HT_6 receptors.

Claims:

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

one of X and Y represents –N= and the other represents –N(R^5)-;

R^1 and R^2 independently represent hydrogen or C_{1-6} alkyl or R^1 is linked to R^2 to form a group $(CH_2)_2$, $(CH_2)_3$ or $(CH_2)_4$;

R^3 independently represents hydrogen, halogen, cyano, $-CF_3$, $-OCF_3$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkanoyl or a group $–CONR^6R^7$;

R^4 and R^5 independently represent hydrogen or C_{1-6} alkyl;

R^6 and R^7 independently represent hydrogen or C_{1-6} alkyl or together may be fused to form a 5- to 7- membered aromatic or non-aromatic heterocyclic ring optionally interrupted by an O or S atom;

m represents an integer from 1 to 4, when m is an integer greater than 1, two R^2 groups may instead be linked to form a group CH_2, $(CH_2)_2$ or $(CH_2)_3$;

n represents 1 or 2;

p represents 1 or 2

A represents a group $–Ar^1$ or $–Ar^2Ar^3$;

Ar^1, Ar^2 and Ar^3 independently represent an aryl group or a heteroaryl group, both of which may be optionally substituted by one or more (eg. 1, 2 or 3) substituents which may be the same or different, and which are selected from the group consisting of halogen, hydroxy, cyano, nitro, trifluoromethyl, trifluoromethoxy, C_{1-6} alkyl, trifluoromethanesulfonyloxy, pentafluoroethyl, C_{1-6} alkoxy, arylC_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkoxyC_{1-6} alkyl, C_{3-7} cycloalkylC_{1-6} alkoxy, C_{1-6} alkanoyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyloxy, C_{1-6} alkylsulfonylC_{1-6} alkyl, arylsulfonyl, arylsulfonyloxy, arylsulfonylC_{1-6} alkyl, C_{1-6} alkylsulfonamido, C_{1-6} alkylamido, C_{1-6} alkylsulfonamidoC_{1-6} alkyl, C_{1-6} alkylamidoC_{1-6} alkyl, arylsulfonamido, arylcarboxamido, arylsulfonamidoC_{1-6} alkyl, arylcarboxamidoC_{1-6} alkyl, aroyl, aroylC_{1-6} alkyl, arylC_{1-6} alkanoyl, or a group $CONR^8R^9$ or $SO_2NR^8R^9$, wherein R^8 and R^9 independently represent hydrogen or C_{1-6} alkyl or together may be fused to form a 5- to 7-membered aromatic or non-aromatic heterocyclic ring optionally interrupted by an O or S atom; or solvates thereof.

2. A compound according to claim 1 which is a compound of formula E1-E5 or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1 or claim 2 for use in therapy.

4. A compound according to claim 1 or claim 2 for use in the treatment of depression, anxiety, obesity and cognitive memory disorders.

5. A pharmaceutical composition which comprises a compound according to claim 1 or claim 2 and a pharmaceutically acceptable carrier or excipient.